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10/588,153	03/02/2007	Itamar Willner	WILLNER9A	3654

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EXAMINER	
VIVLEMORE, TRACY ANN	
ART UNIT	PAPER NUMBER
1635	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/588,153	WILLNER ET AL.	
	Examiner	Art Unit	
	Tracy Vivlemore	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 February 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *11 and 15-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10 and 12-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *01 August 2006* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/10/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *notice to comply*.

DETAILED ACTION

Requirement to comply with sequence rules

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. §§ 1.821-1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Specifically, pages 17 and 22 of the specification contain sequences lacking a sequence identifier and drawing figures 1, 4, 5, 6, 10 and 12 show sequences lacking a sequence identifier either in the drawing itself or the brief description of the figure.

To be considered fully responsive, any reply to this action must correct these deficiencies, as this requirement will not be held in abeyance.

Election/Restrictions

Applicant's election with traverse of group 1, claims 1-10 and 12-14, in the reply filed on February 11, 2009 is acknowledged. The traversal is on the ground(s) that groups 2 and 3 have the same special technical feature as group 1: detection of an analyte. Applicants further argue that claim 1 is a generic claim and therefore the requirement should be for election of species. Applicants additionally argue the requirement is in conflict with *In re Weber*. These arguments are not found persuasive because the special technical feature of groups 2 and 3 is not the same as that of group

1. Group 1 is directed to a method of detecting an analyte in a sample that comprises a step of binding a catalytic polynucleotide to the analyte; the polynucleotide and the analyte interact directly. In groups 2 and 3, the analyte and the polynucleotide do not interact directly. Further, the inventions lack unity of invention because they do not make a contribution over the prior art as described in the rejections that follow. The argument that claim 1 is a generic claim is not persuasive because this assertion is incorrect. As noted in the restriction requirement, although claim 11, for example, depends from claim 1, it recites steps that conflict with the requirements of claim 1. As noted above, claim 1 recites that the catalytic polynucleotide binds the analyte, while claim 11 states that the catalytic polynucleotide does not bind the analyte, but instead binds a member of a complex forming group. Applicants' argument that the restriction conflicts with *In re Weber* is not persuasive because that decision was made with regard to Markush claims, which are not present in the instant application.

The requirement is still deemed proper and is therefore made FINAL.

Claims 11 and 15-20 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on February 11, 2009.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-4 and 7-9 are rejected under 35 U.S.C. 102(b) as being anticipated by Travascio et al. (Chemistry & Biology 1998, cited on IDS).

The claims are directed to a method for determining the presence of an analyte in a sample by contacting a sample with catalytic polynucleotide that binds to the analyte, providing assay conditions to allow the catalytic polynucleotide to produce an optically detectable signal in the presence of the analyte and determining the presence of the analyte in the sample by detection of that signal. In specific embodiments the catalytic polynucleotide is a DNAzyme, the catalytic polynucleotide has peroxidase activity and is complexed with hemin, and the optically detectable signal is production of a colorimetric product such as that produced by ABTS. In another embodiment the method is performed quantitatively by comparing the optically detectable signal with a calibration scale.

Travascio et al. disclose a catalytic DNA sequence that exhibits peroxidase activity when complexed with hemin. Because this sequence binds hemin and is only active after this binding, hemin is considered to be an analyte. Travascio et al. further disclose the use of ABTS as a detectable signal and the use of a calibration curve for quantification of the signal (see materials and methods).

Thus, Travascio et al. disclose all limitations of and anticipate claims 1-4 and 7-9.

Claims 1-3, 5, 7, 9 and 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Usman et al. (US 2002/0102568).

The claims are directed to a method for determining the presence of an analyte in a sample by contacting a sample with catalytic polynucleotide that binds to the analyte, providing assay conditions to allow the catalytic polynucleotide to produce an optically detectable signal in the presence of the analyte and determining the presence of the analyte in the sample by detection of that signal. In specific embodiments the catalytic polynucleotide is a DNAzyme, the catalytic polynucleotide has peroxidase activity, the optically detectable signal is produced by a light emitting reaction or is production of a colorimetric product, and the analyte is a nucleic acid sequence. In another embodiment the method is performed quantitatively by comparing the optically detectable signal with a calibration scale.

Usman et al. disclose nucleic acid sensor molecules that detect an analyte such as a nucleic acid and produce a detectable signal. Use of these sensor molecules is shown in figures 5 and 7, which show the combination of a catalytic nucleic acid and a target nucleic acid. Upon binding of the target, the catalytic nucleic acid is able to enzymatically cleave a reporter sequence and produce a detectable signal (in figure 5, a fluorescent signal). Usman et al. disclose at paragraph 44 that the signal is produced by a reporter molecule, which can be chromogenic (i.e., colorimetric detection), fluorescent, or chemiluminescent. At paragraph 193 Usman et al. disclose that the enzymatic nucleic acid can be a peroxidase. At paragraph 174 Usman et al. disclose

kits for detection of an analyte, one component of which is a standardized solution to be used in making of a calibration curve.

Thus, Usman et al. disclose all limitations of and anticipate claims 1-3, 5, 7, 9 and 13.

Claims 1, 2, 7, 9 and 12 are rejected under 35 U.S.C. 102(b) as being anticipated by Lu et al. (US 2003/0215810).

The claims are directed to a method for determining the presence of an analyte in a sample by contacting a sample with catalytic polynucleotide that binds to the analyte, providing assay conditions to allow the catalytic polynucleotide to produce an optically detectable signal in the presence of the analyte and determining the presence of the analyte in the sample by detection of that signal. In specific embodiments the catalytic polynucleotide is a DNAzyme, the optically detectable signal is production of a colorimetric product, and a plurality of catalytic polynucleotides are bound to a bead-like particle. In another embodiment the method is performed quantitatively by comparing the optically detectable signal with a calibration scale.

Lu et al. disclose (see paragraphs 16-20 and the examples) methods for detecting ions in a sample that comprise the steps of contacting a nucleic acid enzyme (including a DNAzyme)-substrate complex with a sample containing the ion. The ion binds the enzyme, allowing cleavage of the substrate to produce an optically detectable signal in the form of a colorimetric product only when the ion (the analyte) is present. In one embodiment, the enzyme-substrate complex is present as an aggregate of gold particles which produce the colorimetric change by disassociation of the aggregate. At

paragraph 67 Lu et al. disclose that the method can be used for quantitative determination of the ion and at paragraph 77 disclose that kits for use in the method can comprise either standard solutions having known quantities of ion, which the person of ordinary skill would recognize are used to produce a calibration curve, or a standard chart of gold particles in different aggregation states.

Thus, Lu et al. disclose all limitations of and anticipate claims 1, 2, 7, 9 and 12.

Claims 1, 2, 5 and 9 are rejected under 35 U.S.C. 102(e) as being anticipated by Lu et al. (US 6,706,474).

The claims are directed to a method for determining the presence of an analyte in a sample by contacting a sample with catalytic polynucleotide that binds to the analyte, providing assay conditions to allow the catalytic polynucleotide to produce an optically detectable signal in the presence of the analyte and determining the presence of the analyte in the sample by detection of that signal. In specific embodiments the catalytic polynucleotide is a DNAzyme and the optically detectable signal is a light emitting reaction. In another embodiment the method is performed quantitatively by comparing the optically detectable signal with a calibration scale.

Lu et al. disclose (see column 2, line 59 through column 3, line 55 and the examples) methods for detecting ions in a sample that comprise the steps of contacting a nucleic acid enzyme (including a DNAzyme)-substrate complex with a sample containing the ion. The ion binds the enzyme, allowing cleavage of the substrate to produce an optically detectable signal in the form of a fluorescent signal only when the ion (the analyte) is present. In example 3 Lu et al. disclose that the method can be

used for quantitative determination of the ion by comparison of the fluorescent signal with a standard calibration curve.

Thus, Lu et al. disclose all limitations of and anticipate claims 1, 2, 5 and 9.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Travascio et al. as applied to claims 1-4 and 7-9 above, and further in view of Kawaguchi et al. (US 2002/0076696).

Claims 1-4 and 7-9 are described in the 102(b) rejection over Travascio et al. Claims 5 and 6 recite that the optically detectable signal is a light emitting reaction produced by the use of luminol.

The teachings of Travascio et al. are described in the 102 rejection over this reference. Travascio et al. teach the detection of hemin by measuring peroxidase activity of a catalytic DNA using colorimetric detection by ABTS, but do not teach the use of the chemiluminescence of luminol as a means of producing a signal.

However, at the time the invention was made those of ordinary skill in the art were aware that ABTS and luminol were two alternative means for detecting peroxidase activity. See, Kawaguchi et al., who at paragraph 46 teach that when peroxidase is used as a labeling enzyme, reagents for detecting or quantitatively determining the activity of the enzyme include hydrogen peroxide and a color reagent such as 2,2'-azino-bis(3-ethylbenzothiazoline)-6-sulfonic acid (ABTS) or a luminescence reagent such as luminol. Because Kawaguchi et al. teach that ABTS and luminol are functional equivalents used to detect peroxidase activity, one of ordinary skill in the art would find it obvious to use the method of detecting hemin taught by Travascio et al. using luminol detection instead of ABTS and would have a reasonable expectation that this substitution would provide predictable results.

Thus, the invention of claims 1-9 would have been obvious, as a whole, at the time the invention was made.

Claims 1-3, 5, 7, 9, 10, 13 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Usman et al. as applied to claims 1-3, 5, 7, 9 and 13 above, and further in view of Lansdorp (US 2003/0022204).

Claims 1-3, 5, 7, 9 and 13 are described in the 102(b) rejection over Usman et al. Claim 10 recites that the analyte is attached to a solid support and claim 14 recites that the nucleic acid sequence contains a telomere repeat.

The teachings of Usman et al. are described the in the 102 rejection over this reference. Usman et al. teach nucleic acid sensor molecules used to detect nucleic acid sequences and further teach (see figure 23) that the sensor molecules can be attached to a solid surface. Usman et al. do not teach attachment of the analyte to a solid surface and do not specifically teach the detection of nucleic acids comprising telomere repeats.

At the time the instant invention was made, those of ordinary skill in the art were aware that telomeres were comprised of a short, repeating sequence and that the presence of a telomere repeat sequence in a chromosome or fragment was an indicator of the age of a cell. See Lansdorp, paragraphs 2-3.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the nucleic acid sensor molecules taught by Usman et al. in a detection method wherein the analyte is attached to a solid surface. Usman et al. teach that the sensor molecule can be attached to a surface and that these sensors can be used to detect nucleic acid sequences. One of ordinary skill in the art would immediately recognize that such a detection method would also be feasible when the target nucleic acid is attached to the surface in place of the sensor portion. It would further have been obvious to one of ordinary skill in the art to produce a sensor molecule that binds to a nucleic acid comprising a telomere repeat because Lansdorp teaches that such sequences are indicators of a cell's age. Usman et al. teach nucleic

acid sensor molecules that can detect a nucleic acid of any sequence and one of ordinary skill in the art would recognize that designing the sensor to detect sequences comprising telomere repeat sequences requires only the inclusion of the complement of the telomere repeat in sensor component "A" of figure 5.

Thus, the invention of claims 1-3, 5, 7, 9, 10, 13 and 14 would have been obvious, as a whole, at the time the invention was made.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tracy Vivlemore whose telephone number is 571-272-2914. The examiner can normally be reached on Mon-Fri 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz, can be reached on 571-272-0763. The central FAX Number is 571-273-8300.

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